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13. ABSTRACT ***(Maximum 200 Words)***

We completed enrollment of subjects on September 30, 2000 for our nested case-control study of the association between magnetic field and breast cancer risk among a group of predominantly African-American and Latino women in Los Angeles County. The research questions remain as follows:

Primary

1.) Is residential exposure to magnetic fields, as assessed by wiring configuration coding in homes occupied over the past 10 years before diagnosis, associated with the risk of breast cancer. Wiring configuration coding is a method that uses data on the types and distances to nearby outdoor electrical wiring to impute magnetic field levels in homes.

2.) Do higher exposures to alternating current (AC) magnetic fields, as assessed by 7 days of measurements, increase a woman's risk of breast cancer.

Secondary

1.) Do particular combinations of the alternating current (AC) magnetic field and the direct current (DC) magnetic field, increase the risk of breast cancer. The AC field results from our use of the 60 Hz electric power supplied by utilities; the DC (or static) field results from the earth's magnetic field but is altered by the environment within residences. This hypothesis was prompted by observations of biologic effects at particular combinations of the AC and DC fields in several experimental systems.

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INTRODUCTION

Primary Specific Aims:

1. One primary specific aim is to determine if residential exposure to magnetic fields, as assessed by wiring configuration coding, is associated with the risk of breast cancer. Wiring configuration coding is a method that uses data on the types and distances to nearby outdoor electrical wiring to impute magnetic field levels in homes. Specifically, we will test whether subjects who have lived over the past 10 years in homes with wiring configurations associated with higher exposure to magnetic fields have an increased risk of breast cancer.

2. Another primary specific aim is to determine whether higher exposures to alternating current (AC) magnetic fields, as assessed by 7 days of measurements, increase a woman's risk of breast cancer. Measurements will include 6 days of measurements in the bedroom of the current residence and 1 day of personal monitoring.

Secondary Specific Aim:

1. The secondary specific aim is to test the hypothesis that particular combinations of the alternating current (AC) magnetic field and the direct current (DC) magnetic field, increase the risk of breast cancer. The AC field results from our use of the 60 Hz electric power supplied by utilities; the DC (or static) field results from the earth's magnetic field but is altered by the environment within residences. This hypothesis was prompted by observations of biologic effects at particular combinations of the AC and DC fields in several experimental systems. In year two we received supplementary funding from the ARMY to update our exposure assessment protocol to better address this hypothesis. We now use the Multiwave System II to simultaneous make the spot measurements of the AC and DC fields so that we can be sure of their relative orientations.

Significance:

Major differences in breast cancer rates between low incidence countries in Africa and Asia and high incidence countries in Northern Europe and North America (Parkin 1992), as well as the rise in incidence over time (Devesa et al., 1987), suggest that some correlate of industrialization influences breast cancer risk. Although many factors correlate with industrialization, including changing reproductive patterns, increasing exposure to magnetic fields produced by the electric power system could play a role (Stevens et al., 1992). Support for this conjecture comes from the laboratory in the form of a plausible biologic mechanism linking EMF exposure to enhanced risk of breast cancer (Stevens et al., 1992). Central to the hypothesis are laboratory studies of the effects of magnetic field exposure on pineal function, in particular melatonin production (Kato et al, 1993), and the inhibitory effects of melatonin on mammary carcinogenesis (Hill and Blask, 1988). Melatonin, a hormone crucial to regulation of circadian rhythms, also plays a role in control of the reproductive cycle (Tamarkin et al., 1985). In addition, more recent data suggest that magnetic field exposure, at levels close to those observed in homes, may decrease melatonin's inhibitory action on breast carcinogenesis (Liburdy et al., 1993).

While epidemiologic data are sparse, there is evidence that occupational exposure to magnetic fields, as approximated by job title, is a risk factor for breast cancer in both men (Matanowski et al., 1991; Tynes and Andersen, 1991) and women (Savitz and Loomis, 1994, Coogan et al., 1996). Further, there is data that female breast cancer risk is associated with higher residential exposure as assessed indirectly by wiring configuration coding (Wertheimer and Leeper, 1987)

There are laboratory and theoretical data that suggest that certain combinations of AC (time varying) and DC (static) magnetic fields may have enhanced potential for causing biological effects (Blackman and Most, 1993). These are generally referred to as magnetic-resonance hypotheses. While there are few epidemiologic data suitable for examining these hypotheses in relation to cancer risk, one recent study suggests that combinations of the AC and dc field are associated with the risk of childhood leukemia in Los Angeles (Bowman et al., 1995). Because of this exciting result, we included measurements of dc magnetic field in the home to address secondary aim # 2 above.

Methods of approach:

This is a nested case-control study. The base population is a cohort study of African-American and Latino women in Los Angeles County. Exposure assessment is by means of wire configuration coding combined with direct measurements of AC and DC magnetic fields. More detail is found in the Body of this report.

BODY OF THE REPORT

In this study, we are assessing exposure to magnetic fields in three ways:

1. **Wiring configuration coding**, in which data on the types and distances to nearby outdoor electrical wiring (i.e.: transmission and distribution lines) are used to impute magnetic field levels in all homes in Southern California occupied by subjects in the past 10 years. We are using a protocol developed for an NCI funded study of childhood leukemia which has been extensively tested. This is a modification of the Wertheimer Leeper wiring configuration which has been associated with the risk of childhood cancer in a number of studies (Wertheimer and Leeper, 1979) but has not been well studied in relation to breast cancer. Wire coding involves drawing a map of the type of power lines running with 150 ft of the house and their distance from the house (250 for transmission lines).
   The wire coding is being done in a blinded fashion a computer algorithm after specified data are abstracted from the map.

2. **Direct recordings of alternating current (AC) magnetic fields** in the home over 7 days using Emdex magnetic field meters (Enertech Consultants, Campbell CA). The meter takes measurement every 120 seconds. The meter is worn by the subject for the first day and then placed at the bedside. After recording, we download the data to a laptop computer, check and then store the data for analysis.

3. **DC (static) magnetic field measurements** at several locations in the home using the Multiwave System II (ERM, State College PA). These are made along with corresponding spot measurements of the AC magnetic field at three locations in the bedroom (2 locations on the bed--where the subjects' head lies and where the chest lies), as well as in the bathroom, kitchen and living room. The use of Multiwave System II, which we were able to purchase thanks to supplementary funding from the ARMY enables these AC and DC spot measurements to be made simultaneously by the same instrument. This way we are certain of their relative orientation which is important to testing the secondary hypothesis.

A questionnaire regarding residential history and sources of magnetic field exposure at home (such as appliances) as well as history of occupational exposure to magnetic fields and exposure to light at night (a potential confounder) is also administered. The questionnaire was based largely on a questionnaire used in a recently completed study of magnetic fields and breast cancer in Seattle (NCI funded). However, we benefited from feedback from those investigators regarding which questions on their questionnaire did work as well as others.

The study is a case-control study nested within a cohort study of risk factors for breast and other cancers among African-Americans and Latinos in Los Angeles County directed by Dr. Brian Henderson . The cohort study is funded by the National Cancer Institute (CA 54281 – Lawrence Kolonel Principal Investigator). The base population for the nested case-control study consists of the cohort of approximately 74,000 women who are predominately Latino and African-American aged 45-74 years who responded to a 26-page mailed questionnaire which includes information on known risk and suspected risk factors for breast cancer and a detailed dietary history. The cohort was recruited from computer files of the Department of Motor Vehicles (for persons under age 65) and the Health Care Financing Administration (for persons over age 65). The nested case-control study of magnetic fields and breast cancer includes all incident cases of female breast cancer diagnosed within the cohort over 4 years. Women with incident breast cancer are identified through the population based tumor registry for Los Angeles County. Controls are a random sample of women in the cohort who do not have breast cancer. The review of first previous annual report expressed concern over the possibility that some of the controls might really have breast cancer. It is possible that a small number of women, were they subject of mammography, might have breast cancer. However, given the low annual incidence of breast cancer among women as a whole in this age group, we would predict that only a handful of women in the group of over 1000 controls will have breast cancer. This is clearly a trivial form of bias. This potential bias is minimized further because we will know whether a

woman previously enrolled as a control is subsequently diagnosed. So, we can use the appropriate analytic techniques from the literature to deal with this handful of subjects. We have just recently expanded the base population to include women who self-report being non-hispanic white in the cohort who were recruited form the neighborhoods which were identified as predominately Latino. The reason is to ensure enrollment of our target number of cases and controls. The study population remains primarily minority women. Cases and controls are contacted to participate in the measurements and questionnaire. Women who chose not to take the time to actively participate in measurements can be included because exposure can be indirectly assessed by wire configuration coding the home occupied at the time of diagnosis. In addition, data on risk factors for breast cancer are available on all subjects from the baseline cohort study questionnaire.

Quality control:

Emdex meters and magnetometers are formally factory calibrated every 6 months but we calibrate them weekly at the office using equipment designed by our engineering consultant, William Kaune, and thus would identify any faulty machines (no problems to date). Wire coding is done blind to case or control status. Wire coders were trained by William Kaune and adhere to a standard protocol for drawing maps. The actual wire code is assigned by a computer algorithm to eliminate potential bias. Dr. Kaune has designed a calibration unit for the Multiwaves and we calibrate weekly. We will also send the Multiwaves to the factory for calibration yearly. Quality control for wire code entails having a random sample of wire maps redrawn by an experienced mapper, Bob Workley with Enertech Consultants. He did all wire coding for the large NCI funded study of childhood leukemia published this year. We then compare these maps to those of our study mappers and identify any discrepancies and discuss them while at the location. This will be repeated every 6 months. To date we have had excellent concordance. The only minor discrepancies have involved the parameter of thick versus thin wires which is a known weakness of the original Wertheimer Leeper wire code as it is subjective. However, we also use the modified Kaune code which does not use this parameter.

CONCLUSIONS

Key Research Accomplishments:

Subjects

Women from a prospective cohort of African-American and Latino women with no prior history of cancer (other than basal or squamous cell skin cancer) and resided in Los Angeles County at the time of interview were eligible for the study. Initially, women aged 45-74 years old identified from driver's license files for Los Angeles County became part of the cohort upon returning a self-administered questionnaire focused on diet and other lifestyle factors that may influence cancer risk. Cases were cohort members, identified as having breast cancer via linkage with the Los Angeles County Cancer Surveillance Program after their enrollment into the cohort through follow-up on August 9, 1999. Controls were drawn from a random sample of women in

the cohort who had not developed breast cancer. We attempted to frequency matched on self-reported ethnicity using three categories – African-American, Latino and Caucasian.

We attempted to contact a total of 752 eligible cases and 702 controls (Table 1). For subjects who were willing, we scheduled an in-person interview and home visit to make magnetic field measurements. The questionnaire included items on factors that may influence exposure to magnetic fields and light at night. Subjects were asked for the addresses of all homes occupied in the 10 years prior to diagnosis, or a comparable reference date for controls. Controls were assigned a reference date which was the average reference date for cases interviewed during that six month period. The questionnaire also included items on the usual time of going to bed and arising, use of electric appliances and occupations held during the 10 years prior to diagnosis. Data on traditional risk factors for breast cancer such as age at menopause, reproductive history and alcohol intake, were taken from the baseline cohort questionnaire and were not asked at the interview. A total of 657 subjects, 358 cases and 299 controls, were interviewed at home. For subjects who did not agree to a home visit, we offered the interview by phone. A total of 193 cases and 116 controls had an interview by phone. For subjects unwilling to provide a phone interview, we mailed an abbreviated questionnaire containing the residential history and an abbreviated occupational history. A total of 41 cases and 78 controls returned this brief questionnaire.

Wiring configuration

Wiring configurations was used to impute magnetic field in homes occupied for at least 6 months for a reference period that was 10 years prior to the date of diagnosis for cases or corresponding reference date for controls. We were able to wire code at least one home for 744 cases and 700 controls. For subjects that we were unable to contact or who refused to provide an address history, we wire mapped the address from the initial cohort study questionnaire. Only 10 subjects did not have a residence mapped due to bad street address. We were unable to follow-up on these addresses because the subjects were deceased at the time of enrollment, or a hard refusal, or we were unable to trace and contact the subject.

Classification of wire configurations of all eligible residences in Southern California, involved a field technician who drew sketches of the house and all overhead electrical transmission and distribution facilities within 140 feet and substations within 250 feet of the home. We blindly classified wiring configuration according to a simplified Wertheimer Leeper wiring configuration code developed by Savit and Kuane (1993). The homes were classified into one of the following 5 categories – underground, very low current configuration, ordinary low current configuration, ordinary high current configuration and very high current configuration.

Wire mapping was completed by two technicians, who were blind to case or control status. To reinforce adherence to the protocol, every 6-9 months, 20-25 maps were done independently by the two technicians and the results compared and a consensus wire map was reached. Furthermore, a total of 56 homes selected to have approximately equal numbers in each of the 5 wire code categories, were mapped by the two technicians and quality control was reflected in high level of agreement on wire codes.

Magnetic field measurements

We attempted to make measurements in the home that the subject lived in most recently prior to the reference date. We did not attempt to measure homes that the subject had lived in previously. We attempted to make 7 day measurements of magnetic fields in the subjects bedrooms (bedroom meter), obtain 24 hours of personal monitoring using an additional meter (personal meter), and obtain measurements of the static magnetic field in the subject's bedroom at the time that the 7 day meter was placed. After measurements were made on the surface of the bed at the chest location, the bedroom meter was placed on a bedside stand or on the floor under or next to the bed in a location that measured within 0.5 mG of the bed measurement. After the initial 24 hour personal monitoring period, the second meter was placed in the second most frequently used room after the bedroom. A total of 342 cases and 283 controls agreed and completed all measurements. There were 16 additional cases and 16 additional controls that allowed for spot measurements around their homes.

The personal meter was the Emdex Lite and the bedroom meter was Emdex II (both from Enertech Consultants, Campbell CA). Prior to May 1996, the static field measurement was made with a Geometer. From May 1996 on the static field measurements were made using a Multiwave System II (Electric Research and Management Incorporated, State College PA). All meters were factory calibrated every 6-9 months. In addition, each meter was calibrated weekly at the study office.

Reportable Outcomes:

We have examined the relation between the study outcome, breast cancer, and our two major indices of magnetic field exposure, wiring configuration and measured fields.

Wiring configuration

Using the Wertheimer-Leeper wiring configuration classification, we chose to combine the very low and underground categories into a single reference group to provide more stable estimates (Table 2). Nearly identical proportions of cases and controls were in each of the wire code categories from their home at diagnosis. There was no association between risk of breast cancer and the wire code of the diagnosis home.

Magnetic field measurements

Results regarding exposure to nighttime magnetic field are shown in Table 3. Overall, there was no association between risk of breast cancer and any of the following: 1) mean nighttime bedroom magnetic field; 2) proportion of nighttime measurements ≥ 0.2 : T; and 3) short-term variability in nighttime bedroom magnetic field.

Overall, this study so far shows no evidence of an important association between magnetic fields and breast cancer risk. A major strength of this study is the nested case-control design. By using this method, the base population is well defined. For the assessment of wiring configuration, we were able to obtain assessment of exposure on nearly all eligible subjects. This eliminates the possibility of selection bias as an explanation for the results for wiring configuration. Because of our use of the nested case control design, we are also able to characterize subjects who chose not to participate in the measurement component of the study with respect to their baseline questionnaire information.

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Appendices

Table 1: Number of cases and controls enrolled and level of participation in study

			Cases	Controls
Interview Data **Eligible for interview**		**1454**	**752**	**702**
Levels of participation	Interview	**967**	**551**	**416**
	Partial Interview: Proxy Interview or mailed questionnaire, Job and Residential history	**130**	**49**	**81**
	Hard Refusal	**200**	**82**	**118**
	Deceased & Unable to reach	**157**	**70**	**87**
Measurements	Bedroom Magnetic field measurements	**631**	**345**	**286**
	Spot measurements	**661**	**360**	**301**
	Personal Meter monitoring	**596**	**327**	**269**
Wiring Configuration				
	Subjects with at least 1 map completed:	**1444**	**744**	**700**
	Total # of Wire Code residence:	**1726**	**897**	**829**

Table 2. Risk of breast cancer and residential Wertheimer-Leeper wire code, adjustment for confounders, Los Angeles County nested case-control study, 5/93 - 12/99.

	Cases	Controls	Adjusted*	
Wire code variable	No. (%)	No. (%)	Odds Ratio	95% confidence interval
UG+VL	113 (26)	81 (23)	1.00	--
OL	110 (26)	90 (26)	0.95	(0.62, 1.45)
OH	155 (36)	131 (37)	0.91	(0.62, 1.35)
VH	52 (12)	48 (14)	0.84	(0.51, 1.41)

*Logistic regression with the following covariates: age, race, # children, age at first birth, age at first period, height, weight, BMI, age at menopause, HRT, and vigorous activity level.

Table 3. Risk of breast cancer and nighttime[1] bedroom broadband magnetic field, adjustment for confounders, Los Angeles County nested case-control study, 5/93 - 12/99[2].

Broadband exposure variable	Cases No. (%)	Controls No. (%)	------------ Adjusted[4] ------------ Odds Ratio	95% confidence interval
Mean measurement				
Continuous (: T)[5]	249 --	205 --	1.10	(0.91, 1.34)
Quartiles[6]				
1st	51 (20)	51 (25)	1.00	--
2nd	64 (26)	51 (25)	1.68	(0.82, 2.63)
3rd	62 (25)	51 (25)	1.48	(0.80, 2.59)
4th	72 (29)	52 (25)	2.39	(0.89, 2.76)
Quartile as continuous	--	--	1.14	(0.95, 1.36)
Proportion of measurements $\geq$ 0.2 : T				
Continuous	249 --	205 --	1.78	(0.78, 4.10)
Quartiles[7]				
Reference	164 (66)	141 (64)	1.00	--
1st	21 (8)	16 (8)	1.17	(0.57, 2.40)
2nd	18 (7)	16 (8)	1.01	(0.47, 2.19)
3rd	23 (9)	16 (8)	1.38	(0.67, 2.84)
4th	23 (9)	16 (8)	1.31	(0.62, 2.75)
Quartile as continuous	--	--	1.08	(0.93, 1.25)
Any measurement $\geq$ 0.2 : T	85 (34)	64 (31)	1.21	(0.80, 1.86)

Variability (RCM)				
Continuous (: T)[5]	249 --	205 --	1.11	(0.90, 1.37)
Quartiles[6]				
1st	57 (23)	51 (25)	1.00	--
2nd	59 (24)	51 (25)	1.08	(0.60, 1.94)
3rd	59 (24)	51 (25)	1.21	(0.67, 2.16)
4th	74 (30)	52 (25)	1.48	(0.84, 2.60)
Quartile as continuous	--	--	1.14	(0.95, 1.36)
Variability (RCM*)[8]				
Continuous	249 --	205 --	0.72	(0.29, 1.82)
Quartiles[6]				
1st	73 (29)	51 (25)	1.00	--
2nd	43 (17)	51 (25)	0.48	(0.27, 0.87)
3rd	71 (29)	51 (25)	0.77	(0.44, 1.34)
4th	62 (25)	52 (25)	0.77	(0.44, 1.36)
Quartile as continuous	--	--	--	--

[1]10:00 pm to 5:00 am
[2]Includes only those subjects with data available for all covariates used in adjusted analysis.
[4]Logistic regression with the following covariates: age, race, # children, age at first birth, age at first period, height, weight, BMI, age at menopause, HRT, and vigorous activity level.
[5]Log-transformed.
[6]Based on controls only.
[7]Based on controls only with proportion > 0; reference is proportion = 0.
[8]RCM* = standardized RCM

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